

WOOD (H.C.) & HARE (H.A.)

THE CAUSE OF DEATH FROM CHLOROFORM.

✓
BY

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PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS IN THE UNIVERSITY
OF PENNSYLVANIA,

AND

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DEMONSTRATOR OF THERAPEUTICS.



FROM
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February 22, 1890.



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IN the *Indian Medical Gazette* for February, 1889, it is stated that a Commission composed of Dr. Hehir, Mr. Kelly, and Mr. Chamarette, assisted by the students at the Hyderabad Medical School, have made a series of experiments upon 128 full-grown pariah dogs, to ascertain the method in which chloroform causes death. It is further affirmed that the investigators varied the doses and the method of administering the chloroform in every way, and tested the value of artificial respiration by reviving the dogs over and over again, after breathing had stopped, and while the heart was still beating, and that they found that no matter in what way the næsthetic was given the heart became dangerously affected only when the breathing had ceased.

We have not had the opportunity of seeing the original report of this Commission, but learn from current medical journals that under the auspices of



the Nizam of Hyderabad, Dr. Lauder Brunton, of London, has gone to investigate the matter. It is also stated in the *Lancet* that cablegrams have been received from Dr. Brunton affirming that the experiments of the Commission have been verified and their conclusions justified, and that as many as 450 animals have been used in the study of the question.

The surprising statements which have been made in the Indian journals and in the London *Lancet*, with the practical deductions which *apparently* follow upon them, seem to us of so great import as to demand the putting upon record of our own experience.

We believe that physiologists in general hold the opinion that when chloroform is given to the lower animals in a very dilute form, and gradually pushed, it causes by its action upon the nerve centres a paralytic relaxation of the muscles and at last death by paralysis of the respiratory centres; but that when it is administered freely in concentrated vapor by inhalation, or when it is injected in sufficient amount into the jugular vein, it kills by a paralytic arrest of the heart, the viscus stopping suddenly in its beat, and being found after death relaxed and incapable of reacting to stimuli. It has generally been believed that the danger from cardiac arrest by chloroform increases in direct ratio with the rapidity of administration; but that in animals, as well as in man, cardiac arrest sometimes occurs almost at once on the inhalation of the anæsthetic in small amount; or, in other words, that comparatively small amounts of chloroform have at times caused death by syncope, through direct action

upon the heart. This we believe has been the teaching of all the instructors, both clinical and physiological, in the Medical Department of the University of Pennsylvania, and we desire to reiterate, as the result of our past experiences, that chloroform does, in the ordinary American dog, sometimes kill by paralyzing the heart, such paralysis accompanying or preceding, according to our past experiments, the arrest of the respiration.

It has been the custom of one of the authors of this paper, in his lectures before the University class, to demonstrate by means of the respiratory tambour, the mercurial manometer, and the kymographion, a continuation of respiratory movements after cardiac arrest through chloroform. Further than this, we have at various times in the Laboratory of Experimental Therapeutics, at the University, taken tracings proving the same facts.

Moreover, on experimenting with other drugs in the laboratory, the point at issue has been determined, because we almost invariably kill the dog which has escaped the drug being studied, with chloroform, whilst its artery is still attached to the kymographion, and the needle is still registering the play of the blood. We have sometimes given the drug intravenously, but in many cases we have administered it by inhalation of the concentrated vapor, and we have often noticed that death has been produced by primary cardiac arrest.

When chloroform is injected into the jugular vein it is carried first in its concentrated form to the right side of the heart, and when it is absorbed

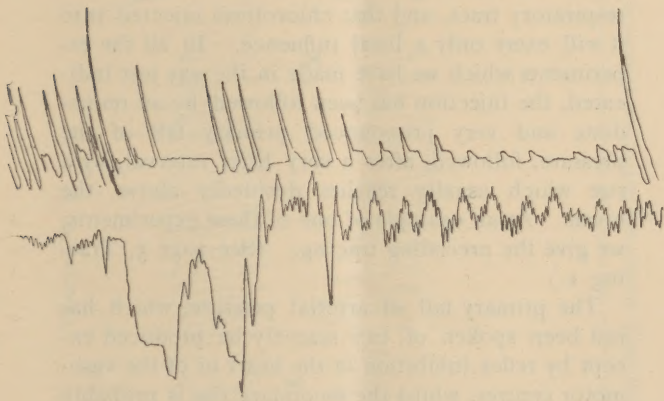
through the lungs it is carried directly to the left side of the heart. In either method of administration the anæsthetic reaches the heart in a concentrated form before it is scattered in the circulation and gets to the respiratory centres. This may have connection with the frequent early occurrence of cardiac arrest during chloroformization in the human subject, but we desire especially to emphasize the point, that in either method of administration the heart is first reached, and that in our experience there is no essential difference in the action of chloroform, whether it is given by inhalation or whether it is injected into the jugular vein.

As we use between us, in the laboratory of the University, many dogs yearly, a very large proportion of which are finally killed by chloroform, we may be excused for our past positive assertions that chloroform is a cardiac paralyzant and does kill dogs by a direct action upon the heart or its contained ganglia; especially since we have been strengthened in our opinion by the fact that Dr. Reichert, Professor of Physiology in the University, has reached results confirming our own, and has frequently demonstrated the same to the University classes.

The statements that have been recently made in the Indian journals and in the London *Lancet*, have led us to reëxamine the subject and to make a series of experiments upon it with the greatest care. We have, also, varied and extended these experiments in order to determine whether chloroform paralyzes

the heart by a direct influence or by an indirect action through the vagus.

A number of our experiments have been made by injecting the chloroform into the jugular vein; in others it has been administered by the respiratory

TRACING No. 1.¹

tract. In all cases accurate tracings have been made by means of the kymographion and the respiratory tambour.

The theory has from time to time found advocates

¹ The upper tracing represents the respirations as registered by a tambour; the second one the pulse waves, and the third the abscissa line and second marks.

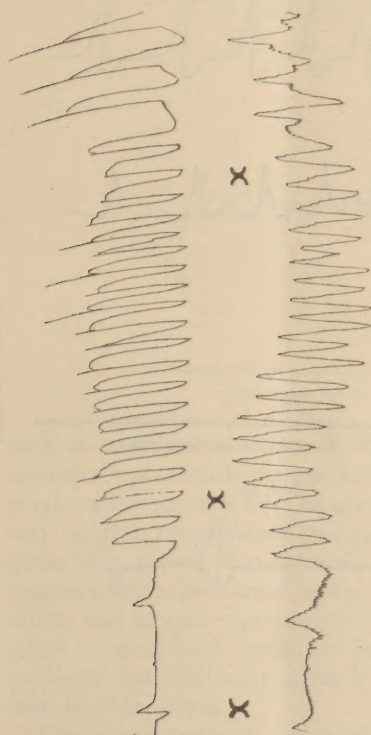
that the vapors of chloroform may, by irritating the larynx and adjacent parts, cause arrest of the heart through a reflex inhibition. To test the possibility of this we have made a number of experiments. When the tracheal canula is tied tightly into the trachea some distance below the larynx, it is evident that the latter organ is isolated from the general respiratory tract, and that chloroform injected into it will exert only a local influence. In all the experiments which we have made in the way just indicated, the injection has been followed by an immediate and very pronounced primary fall of the pressure, followed, after a very brief interval, by a rise which usually reaches decidedly above the norm. As an example of one of these experiments, we give the preceding tracing. (See page 5, Tracing 1.)

The primary fall of arterial pressure, which has just been spoken of, can scarcely be produced except by reflex inhibition of the heart or of the vaso-motor centres, whilst the secondary rise is probably the result of a reflex vaso-motor spasm. In order to throw light upon this question, we have made experiments by injecting chloroform into the larynx after division of the pneumogastric nerves, the trachea being ligated so as to prevent the entrance of the anæsthetic into the lungs. (See page 192, Tracing 2.)

In making practical application of the experiments just discussed, it must be noted that in no case have we succeeded in completely arresting the heart's action by injecting chloroform into the larynx, and as the chloroform was injected in liquid form, it is

plain that the irritation was more intense than could be produced by the mere vapors of the anæsthetic

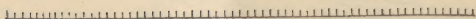
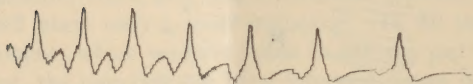
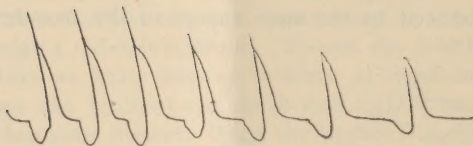
TRACING No. 2.



Vagi cut at first x mark; chloroform injected into larynx from x second to third x marks

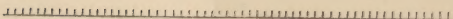
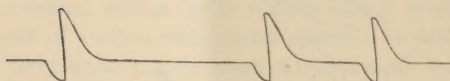
however concentrated; therefore, while it must be considered that it is possible for a reflex inhibitory arrest of the heart to occur during the inhalation,

No. 2a.



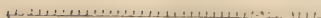
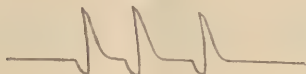
Same continued; no break in time.

No. 2b.



1 minute later.

NO. 2c. -



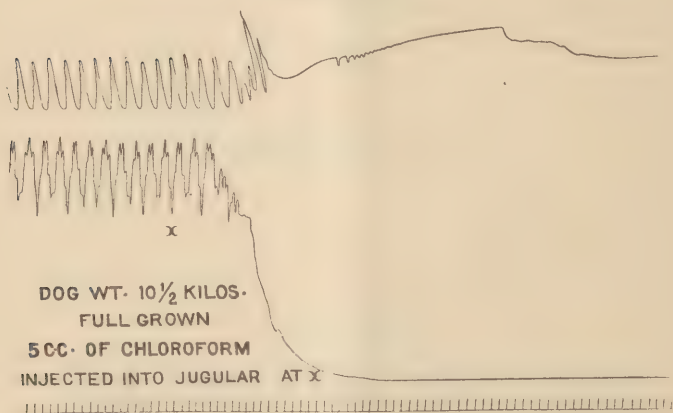
30 seconds later.

such an accident is extremely improbable, and we consider it practically certain that a heart so arrested would, a few seconds later escaping from the inhibitory control, recommence its beat. It certainly has never been proven that chloroform can cause in the human subject permanent reflex inhibitory cardiac arrest, and as our experiments upon the dog have failed to cause such arrest, we consider it very improbable that inhibitory arrest is ever produced in man by chloroform.

The second series of our experiments were made to determine the way in which large amounts of chloroform, either thrown into the jugular vein or absorbed into the pulmonic capillaries, cause death.

We have found that it is possible for the heart and respiration to be practically simultaneously paralyzed by the anæsthetic. (See Tracing No. 3.)

TRACING NO. 3.

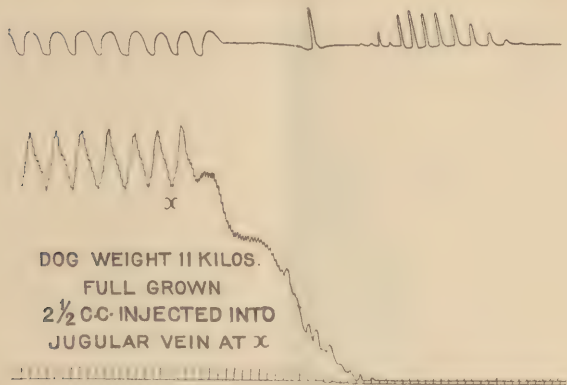


On the other hand, the heart may be arrested during chloroformization, and the respiration continue, as is shown in the accompanying tracings. (See Tracing No. 4.)

We desire to call attention to the fact, that of the two tracings here inserted, one (Tracing No. 4) was made by injecting the chloroform into the jugular vein, whilst the other (Tracing No. 5) was obtained by the inhalation of chloroform. In the second experiment (inhalation) *breathing continued two min-*

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TRACING NO. 4.



utes after the heart had ceased to act. (See page 12, Tracing 5.)

The next series of experiments were made with small doses of chloroform. In a number of these cases the respiration ceased long before the heart's action, as is shown in the appended tracings, in which the heart continued to beat two minutes after the cessation of respiration. (See pages 14 and 15, Tracings 6 and 7.)

The final series of experiments we made to determine whether chloroform arrests the heart by indirectly affecting the vagus or by a direct action upon it. In one experiment (Tracing No. 8, page 17) the vagi were cut before, in the other (Tracing No. 9, page 18) after the exhibition of the chloroform. It is evident that the vagal section has little or no in-

TRACING No. 5.

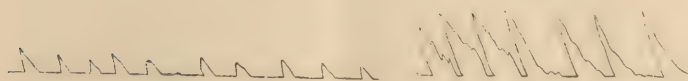


Chloroform inhaled at 8.

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No. 5a.

No. 5b.



Same tracing continued 30 seconds later.

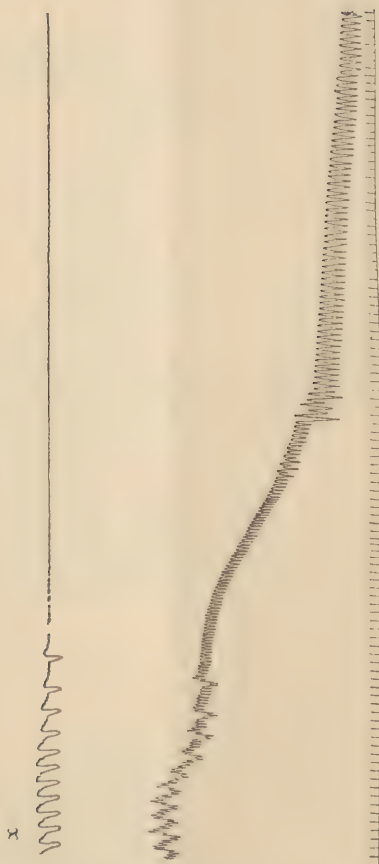
Same continued 1 minute later.

No. 5c.

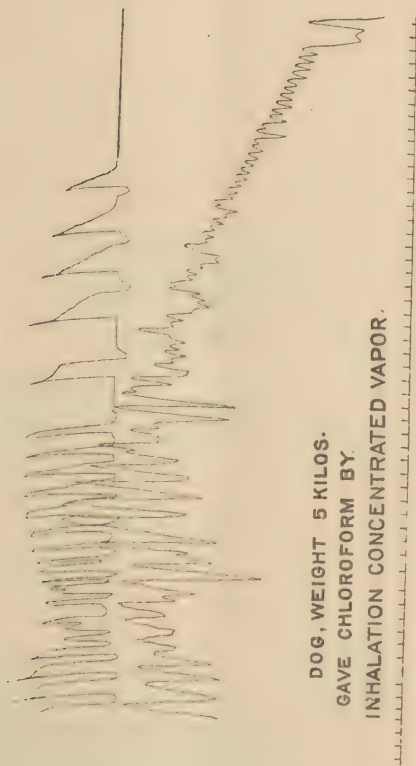


Same continued 30 seconds later.

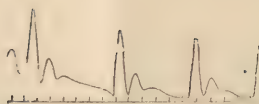
TRACING No. 6.



TRACING No. 7.

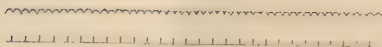


No. 7a.



Same tracing continued, no break in time.

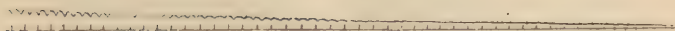
No. 7b.



Same tracing continued 30 seconds later.

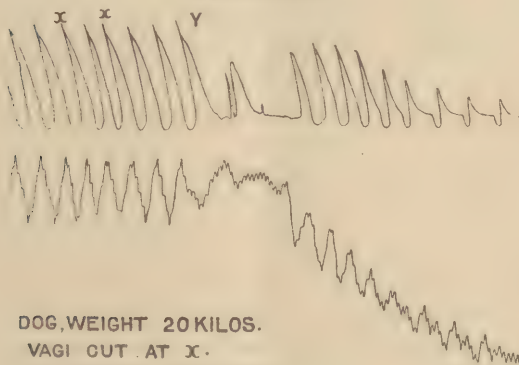
CAUSE OF DEATH FROM CHLOROFORM. 17

No. 7c.



Same tracing continued 1 minute and 30 seconds later.

TRACING NO. 8.



DOG, WEIGHT 20 KILOS.

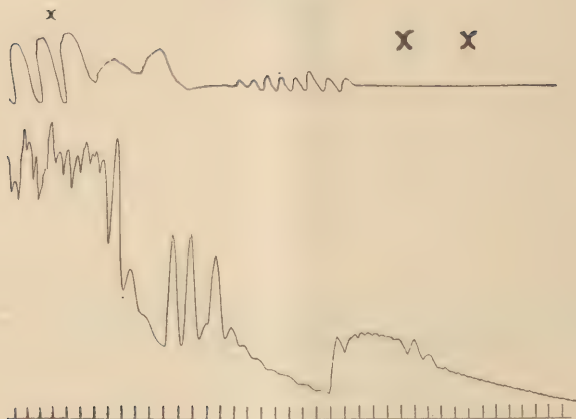
VAGI CUT AT X.

CHLOROFORM INJECTED

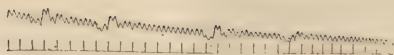
INTO JUGULAR AT Y.



TRACING NO. 9.



Vagi cut at x x, but did not start heart beating again.



Same tracing 1 minute later.

fluence upon the cardiac action of chloroform, which, therefore, acts directly upon the heart and vaso-motor system. (See Tracings 8 and 9.)

The experiments which we have given show that chloroform acts as a powerful depressant poison upon both respiration and circulation, that sometimes the influence is most felt at the heart, and death results from cardiac arrest; that in other cases the drug paralyzes primarily the respiratory centres, whilst in other instances it seems to act with equal force upon both medulla and heart. So far as practical medicine is concerned, it makes little difference whether the heart stops just before or just after respiration; so that those cases, in which cardiac and respiratory arrest are almost simultaneous, are, for the purposes of the clinician, the same as those in which heart-arrest precedes respiratory paralysis. Finally, the general results of our new experiments also coincide with our previous experience in the laboratory, and with what we believe to be the general belief of physiologists—that cardiac arrest is specially prone to occur when chloroform is administered rapidly and in a concentrated form.

The present series of experiments which we have made with chloroform are so concordant in their results with those previously obtained by other experimenters and by ourselves, that it seems to us that their results cannot be gainsaid. Therefore if a final statement should be made by Dr. Lauder Brunton and his India coadjutors that the dogs of India are killed by chloroform solely by the action upon the respiratory centre, the conclusion must be

drawn that the pariah dogs of India are affected by chloroform differently from those of Europe and America. This to us seems the best explanation of the curious results obtained in India. It is possible that the climatic influence of that country may make the respiratory centres abnormally sensitive to chloroform. That the thought of the different constitutions of animals in different climates is not absurd, is shown by the fact that, some years ago—after one of us had stated before the Physiological Section of the International Medical Congress, at London, that if certain asserted results were obtained upon European dogs, said dogs must differ from those of America, and had been met with a smile of incredulity—Dr. Brown-Séquard rose and stated that he had experimented upon hundreds of dogs on both continents, and that there was a distinct difference between the animals, the vascular system of the European dogs being much more developed and operations upon them being, therefore, much more bloody than was the case with the American dog. Hashish causes the East Indian to run amuck and commit crime but fails so to affect the European. Whatever explanation we may accept of the different results which have been reached, we very strongly urge the consideration that these results show that the action of chloroform upon the human system is not to be estimated solely by any influence which it may have on the dogs of India. Indeed, it is possible that there may be the same difference between man in hot and cold climates as there appears to be in dogs in hot and cold climates ;

but we do not know of any statistics which will throw light upon such a supposition. A fact to be remembered is that though 450 pariah dogs in India have died of respiratory failure, an equal number in America have died of cardiac arrest, whilst the records of clinical medicine show that death in the human being from chloroform usually takes place either by primary arrest of the heart, or by a simultaneous arrest of the heart and the respiration, while in etherization the respiration usually ceases distinctly before the heart's beat. We do not propose in the present paper to reiterate the statistics which may be found in the text-books and recent treatises on anæsthetics, but we do desire to say emphatically that we believe the roll of deaths from chloroform would be very much larger if all the cases were reported, and that the present inequality between the anæsthetics, ether and chloroform, would be much more pronounced if an absolutely clear record could be obtained. One of us has seen, in a Philadelphia hospital, death produced by chloroform through cardiac arrest. The other has personal cognizance of two cases; but none of these instances have been reported. The surgeon who uses ether knows that he will receive no blame if a death occurs from it, and also that he has a rare case to put on record, which will give his own name a permanent place in anæsthetic literature, and consequently he naturally hastens to publish his unfortunate result; whereas the surgeon who uses chloroform knows that if death occurs from the anæsthetic, a very large proportion of the profession will condemn him

either in public or secret for the use of this drug. Moreover, deaths from chloroform are only too common, so that the surgeon has nothing to gain and much to lose by publication of a chloroform death, and if possessed of the average human nature, holds his peace.

After the present paper had been sent for publication, the issue of the London *Lancet* for January 18, 1890, came to hand, and we have carefully read the report of the Hyderabad Commission. The great respect and friendship which we have for some of the members of this commission—make us loath to differ from them, but the issue between us is not simply a scientific matter, which would allow of silence, but is of such immense practical importance, involving, as it does, human life, that we feel it a duty to speak.

In the first place, we fear that the Commission's statement that their object is "to *test* the suitability and safety of chloroform as an anæsthetic," will mislead the minds of readers as to the proper scope of experiments upon animals in regard to therapeutic questions. We believe that no one will accuse us of attempting to diminish the importance of such experimentation, but we insist that the only proper objects of such experiments are to lead the way to clinical studies, and to explain clinical facts. A well-established clinical fact cannot be disproved by any amount of experiments upon animals.

We have given elaterium to dogs until it has caused death, but it has not purged. Suppose that every dog in India had had administered to it elaterium, without the production of purgation, would

that prove that elaterium does not purge man? We believe that it is proven by clinical experience that, occasionally, in man chloroform does suddenly, without warning, arrest the heart's action. It seems to us scarcely possible that such conclusions as clinical reports, appear to be too definite and positive upon this point to be contradicted by experimental studies. But we believe that in verity the results of experiments with chloroform upon the lower animals are in accord with those obtained in human medicine.

In any discussion with wide differences of opinion, it is a matter of importance to determine points of agreement as well as of disagreement, and the probability of the correctness of the facts agreed upon is very great. We notice, therefore, with pleasure, that the Commission state (paragraph 18, p. 155): "The theory which has hitherto been accepted is that the danger in chloroform administration consists in the slowing or stoppage of the heart by vagus inhibition. This is now shown to be absolutely incorrect." This is in accordance with our own experimental results and conclusions, and whilst we deprecate the extreme positiveness of assertion, we think it highly improbable that chloroform ever kills man by a reflex inhibition of the heart.

In paragraph 20, p. 155, the Commission further states:

"In experiment ninety-two, repeated injections of twenty minims of chloroform were made into the jugular vein, and their effect was not to paralyze the heart, but to produce anæsthesia and a gradual fall of blood pressure, exactly as if the chloroform had

been inhaled." This statement agrees with what we have already asserted in this paper. Chloroform possesses its peculiar properties by virtue of its inherent nature, and the method of administration does not altogether dominate the effects of the drug, so that conclusions can be predicted upon experiments made by injection into the jugular vein as well as upon those in which the chloroform is administered by inhalation. The agreement of the Commission with ourselves seems, therefore, to cut off any objections to our method of experimentation, especially since in every instance we have tracings obtained by inhalation as well as by injection.

In any discussion it is very important that the essential point be closely adhered to, and not lost sight of in side issues. In the report of the Hyderabad Commission there is a great deal that is novel and of much scientific interest concerning the effects of strangling, of suffocation, of vagi-irritation, etc., upon a chloroformized animal. These are in themselves very valuable, but they are liable to obscure the one main issue—an issue which, fortunately, is tersely expressed by the Hyderabad Commission in a single line, when it says: "and, however concentrated the chloroform may be, it never causes sudden death from stoppage of the heart."

In considering this main issue, we desire, first, to call attention to the fact that the evidence of the Commission is negative, whilst our evidence is positive, and we believe it is a general law of evidence that negative testimony cannot stand against positive when the latter is trustworthy. The Commission

in substance assert: We have made a large number of experiments upon Indian animals, without ever having seen the heart arrested by chloroform before the respiration—therefore, chloroform never causes death by syncope; or, to put it in another way, we have not seen a certain phenomenon, therefore that phenomenon never occurred. On the other hand, we state that we have seen this phenomenon repeatedly, and we offer in proof of our statement, not merely our own assertions, but tracings which have the same relation to physiology that the photograph has to the original transactions of life.

Further, our results in conclusion are in accord with those obtained by other observers since Glover, in 1842, first pointed out that the vapor of chloroform, when locally applied to the exposed heart, stopped its movements. The English Chloroform Commission—Gosselin, Anstie, Richardson, Ringer, and Vulpian—are among the names from whom the Hyderabad Commission appears to differ, and with whom we agree more or less closely.

Much as we differ from the Hyderabad Commission as to the conclusions which should be drawn from their experiments taken in conjunction with those of other investigators, we would dissent much more strongly from the language used by the *Lancet* itself, in its editorial of January 18th, where it says: "The practical outcome of the research would appear to be that deaths from chloroform are not inevitable. They are, therefore, preventible, and *by due care* in its administration *they may be with certainty avoided.*"

We desire most emphatically to protest against

any such language being considered as justified by the work of the India Commission. If, with due care in administering chloroform, accidents may with certainty be avoided, they are, when they do occur, the result of ignorance or carelessness, and the coroner's jury, in a given case, could scarcely, under the rulings of the *Lancet*, fail to bring an accusation of manslaughter against the surgeon. We cannot help wondering if the editor of the *Lancet* appreciated the force of his own words.

According to the latest edition of Dr. Lawrence Turnbull's work on *Anæsthesia*, 375 deaths from chloroform have been recorded. If the unreported cases are borne in mind, it must be considered that at least 500 surgeons have had in their practice fatal accidents during chloroform anæsthesia; the actual number of those who have met with fatal results is probably far greater, and among these surgeons we note these names:

Professors Billroth, Dumreicher, and Jaeger, of Vienna; Sir J. Y. Simpson, Sir George H. B. McLeod, Mr. J. Farrant Fry, and Mr. Francis W. Clark, of England and Scotland; Drs. Hunter McGuire, J. H. Wellford, and Dr. Chancellor, of Virginia; Drs. W. A. Hammond, A. J. Parsons; and Professors W. W. Dawson, Kinloch, and Mussey.

Does the *Lancet* mean to charge that these accidents could have been avoided? That these men have been practically guilty of taking life through carelessness?

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